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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,122	11/22/2006	Axel Bouchon	RCK-62	5546

35969 7590 10/16/2008

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EXAMINER	
LEESER, ERICH A	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
10/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,122	BOUCHON ET AL.	
	Examiner	Art Unit	
	Erich A. Leeser	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-5* is/are allowed.

6)☒ Claim(s) *6-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-31-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19 are pending and under examination.

Priority

Acknowledgement is made that this application is a 371 of PCT/EP04/10606, filed on September 22, 2004, which claims the benefit of EPO 03022235.0, filed on October 1, 2003 and EPO 03025570.7, filed on November 8, 2003.

Information Disclosure Statement

The references contained in the IDS dated March 31, 2006, are made of record.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 14-16 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. V. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 10, and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating specific diseases, does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the tetrahydro-naphthalene and urea derivative compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims". *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150; *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before onset occurs. This would require extensive and potentially open-ended clinical research on healthy subjects. 2) Claims 9-13 list the diseases Applicant intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to clinical neurological medicine and are therefore physiological in nature. 5) The state of the art is that no general procedure is

art-recognized for determining which patients generally will become afflicted before the fact. 6) The artisan using Applicants invention would be a Board Certified physician in neurological diseases with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of CNS diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent CNS diseases generally. That is, the skill is so low that no compound effective generally against CNS disorders has ever been found let alone one that can prevent such conditions. 7) It is well-established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by formula (I).

The Examiner suggests deletion of the word "prevention".

Claims 8-13 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compounds to treat an urological disorder or disease, pain, or an inflammatory disease or disorder using an effective amount of a compound corresponding of formula (I) or enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention:

The instant invention is drawn to tetrahydro-naphthalene and urea derivatives which allegedly have vanilloid receptor (VRI) antagonistic activity, including methods to treat an urological disorder or disease, pain, or an inflammatory disease or disorder using an effective amount of a compound corresponding of formula (I).

The state of the prior art:

The prior art at the time the invention was made tends to show the unpredictability and inconsistency regarding the use, function, and relevant activity of VRI antagonists: "The antihyperalgesic activity of capsazepine observed in guinea pigs is in marked contrast to its lack of effect in mice and rats, where no antihyperalgesic activity was observed in either the neuropathic or inflammatory models." The scientists concluded that: "These data show that VR1 antagonists have antihyperalgesic activity in animal models of chronic inflammatory and

neuropathic pain, and illustrate species differences in the *in vivo* pharmacology of VR1 that correlate with differences in pharmacology previously seen *in vitro*." (Emphasis added). Walker, et al., *The VR1 Antagonist Capsazepine Reverses Mechanical Hyperalgesia in Models of Inflammatory and Neuropathic Pain*, J. of Pharm. and Exper. Ther., Vol. 304, No. 1, pp. 56-62 (2003).

The predictability in the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the claimed invention is highly unpredictable since one skilled in the art would not necessarily recognize, with regards to therapeutic effects, whether or not the compounds of formula (I) would be useful to treat an urological disorder or disease, pain, or an inflammatory disease or disorder.

Amount of guidance/working examples:

Beginning on page 30 Applicant provides "EXAMPLES" ending on page 39. These examples in the specification; however, do not definitively prove that the instant compounds can effectively be used to treat an urological disorder or disease, pain, or an inflammatory disease or disorder using an effective amount of a compound corresponding of formula (I).

The breadth of the claims:

The breadth of claims in claims 41-44 are overly broad as they do not recite specific diseases or disorders, but simply classes of diseases or disorders generally; i.e., an urological

disorder or disease, pain, or an inflammatory disease or disorder. Claims 9, 11 and 13 are not unduly broad as they are limited to the specific diseases.

The quantity of undue experimentation needed:

Since the guidance and teaching provided by the specification is insufficient to effectively treat an urological disorder or disease, pain, or an inflammatory disease or disorder with an effective amount of a compound of formula (I), one of ordinary skill in the art, even with a high level of skill, is unable to use the instant compounds to effectively treat an urological disorder or disease, pain, or an inflammatory disease or disorder as claimed without undue experimentation.

The level of the skill in the art:

The level of skill in the art is high. Due to the unpredictability in the pharmaceutical art; however, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases or diseases would benefit from this activity.

Taking all of the above factors into consideration, it is not seen how one of ordinary skill in the art would be able to use the compounds of formula (I) to treat an urological disorder or disease, pain, or an inflammatory disease or disorder without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) Claims 6-10 and 12 lack antecedent basis as claim 4 is a process claim not a medicament claim. Correction is required.

ii) Claim 11 simply does not make sense. It appears that Applicant intended instead to state "claim 10"? Correction is required.

iii) Claim 11 is unclear because of the word, "realted". It appears as though Applicant intended "related" instead. Correction is required.

iv) Claim 13 simply does not make sense. It appears that Applicant intended instead to state "claim 12"? Correction is required.

v) Claims 14-16 provides for the use of "compounds according to claim 1 for manufacturing a medicament", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

vi) Claims 17-19 are unclear because they do not follow standard U.S. practice. Examiner recommends "Process for controlling …" be amended to "A method of treatment …".

Allowable Subject Matter

Claims 1-5 are patentable over the closest prior art, seen to be Rami, et al., WO 03/068749. The difference between the compounds of the WO patent and the instant compounds is that the patent's corresponding position to instant Q_{2A} must be nitrogen instead of the instant carbon. Therefore, the claims are seen to be free of prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leeser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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